IN THE UNITED STATES DISTRICT COURT FOR THE WESTERN DISTRICT OF OKLAHOMA

BETTY ANN MARSEE, Administratrix of the Estate of MARVIN SEAN MARSEE, Deceased,	)	
Plaintiff,	)	
vs.	)	No. Civ-84-2777R
UNITED STATES TOBACCO CO., a New Jersey corporation,	)	
Defendant.	)	

TRANSCRIPT OF JURY TRIAL PROCEEDINGS
Monday, June 2, 1986

Appearances:

HON. DAVID L. RUSSELL,
U.S. District Judge, Presiding

GEORGE W. BRALY, Esquire
DANIA DESCHAMPS-BRALY, Esquire
Braly & Braly
217 North Mississippi
Ada, Oklahoma 74820
Appeared for Plaintiff.

TIMOTHY M. FINNEGAN, Esquire
Jacob, Medinger & Finnegan
1270 Avenue of the Americas
Rockefeller Center
New York, N.Y. 10020
and
ALSTON JENNINGS, Esquire
Wright, Lindsay & Jennings
2200 Worthen Bank Building
Little Rock, Arkansas 72201
and
ANDY COATS, Esquire
Crowe & Dunlevy
1800 Mid-America Tower
Oklahoma City, OK 73102
Appeared for Defendant.

Volume 16

Maynard E. Peterson, CSR
Acting Official Reporter

BE IT REMEMBERED, that on the 2nd day of June, 1986, the above matter coming on for jury trial before the Honorable David L. Russell, United States District Judge for the Western District of Oklahoma, and the parties appearing in person and or by counsel as hereinabove set forth, the following proceedings were had:

THE COURT: Good morning, ladies and gentlemen. Sit down.

The plaintiff may call your next witness.

MR. BRALY: Your Honor, if it please the Court, this morning we would call Doctor William Lijinsky.

WILLIAM LIJINSKY, PH.D.,

called as a witness on behalf of the plaintiff, being first duly sworn, testified as follows:

DIRECT EXAMINATION

BY MR. BRALY:

Q. Doctor Lijinsky, state your full name, please.

A. William Lijinsky.

Q. Where do you reside, sir?

A. I reside in Frederick, Maryland.

Q. What is your occupation?

A. I am -- I was a cancer biochemist. I am presently director of the Laboratory of Chemical and Physical Carcinogenesis at Frederick Cancer Research Facility in Frederick, Maryland.

Q. Doctor Lijinsky, describe to us a little bit what the function of the Frederick Cancer Research Center is.

A. It's really a branch of the National Institutes of Health. There are activities there mainly in basic and some clinical research on principally cancer, among other diseases.

Q. Is that facility funded entirely by the United States Government?

A. Yes, it is.

Q. Doctor Lijinsky, when did you start working as a scientist?

A. I received my undergraduate degree in 1946, and I then entered graduate school, so I consider I started working as a scientist when I did -- when I started to do research as a graduate student in 1946.

Q. Are you a United States citizen?

A. No, I'm not.

Q. What nationality are you?

A. I'm a citizen of the United Kingdom.

Q. When did you first come to the United States in connection with your research?

A. I came in the winter of 1951, that is, the beginning of 1952.

Q. And what kinds of research did you engage in during the 1950's?

A. I began in California Institute of Technology as a postdoctoral fellow, studying polycyclic aromatic hydrocarbons.

Q. Go ahead.

A. And in addition -- well, I had two main projects: one, study polycyclic aromatic hydrocarbons, and the other was studying substance called carotenoids, which are pigments of plants.

Q. And after you left Cal Tech, where did you go from there?

A. I went to the McGill Montreal General Hospital Research Institute in Montreal. I had a Damon Runyon research fellowship, specifically to study cancer.

Q. All right. Now, you mentioned that you were studying polycyclic hydrocarbons?

A. Yes.

Q. Are those chemicals that cause cancer?

A. Yes, they are.

Q. Now, you have gone to -- did you say Montreal?

A. I went to Montreal for a year on a fellowship, another fellowship.

Q. Any other principal research activities during the 1950's?

A. I went to -- to the Chicago Medical School in Chicago, which is not the University of Chicago. It is a private medical school in Chicago, and there I joined the division of oncology, which is the study of tumors or cancer, and there I worked on tumor-promoting agents and polycyclic aromatic hydrocarbon carcinogenics.

Q. All right. When did you first start to work with and become involved in nitrosamines?

A. In -- sometime during 1959. We had a visit from a man named Peter McGee who really -- he discovered the carcinogenic effect of nitrosamines, and he came to visit -- he was a friend of the director of the division of oncology named Doctor Philip Shubick, and I spent considerable time talking to him during his stay about this new class of water soluble carcinogens called nitrosamines, because

polycyclic hydrocarbons are difficult to work with in studying mechanisms by which they induce cancer, because they are not water soluble. It is hard to study their biochemistry.

Q. Since 1959 have you pursued your studies of nitrosamines?

A. Yes.

Q. Have they occupied a significant portion of your research efforts?

A. A majority of my research time, my research effort.

Q. And, Doctor, before we go on, have you ever consulted in other matters related to litigation?

A. I'm sorry. I didn't --

Q. Have you ever consulted or testified in other matters involving lawsuits?

A. Yes, I have.

Q. In that connection is it customary for you to be compensated for the time that you spend in connection with those matters?

A. Yes, it is.

Q. And have you agreed or have I agreed to do that in this instance?

A. You have. The agreement is because I use my vacation time to appear in such cases.

Q. You are not here on the government's time?

A. No, I am not here on the government's time. I took vacation.

Q. And, Doctor, let's kind of bring us down to date. The NCI-Frederick Cancer Center, what kinds of research do you do there?

A. I work principally on the mechanisms of carcinogenesis by nitrosamines.

Q. Are you published in the medical literature on the subject of nitrosamines?

A. Yes, I have about probably 220 published articles on nitrosamines.

Q. Just on nitrosamines?

A. Just on nitrosamines.

Q. Other articles or other subjects?

A. Yes.

Q. And, Doctor, what is the National Toxicology Program?

A. It's an organization that is -- that was set up by the government to investigate potential carcinogenicity, cancer-causing effect of chemicals that are in common use.

Q. And does it test a number of different chemicals?

A. Yes.

Q. How long has that program been going on?

A. Since about 1972 or -3, I think. I don't know the exact date, but about that it began.

Q. Have you participated in those tests of chemicals for carcinogenicity as a part of that program?

A. Yes, some of them I have tested in my laboratory.

Q. You have done some of those before?

A. Yes.

Q. In what form are those matters published? They are published usually as technical reports, quite detailed technical reports, describing the way the -- the choosing of the background, the background of its chemistry, the way it was tested, and the results, and often conclusions, but not always conclusions, as to the carcinogenicity of the chemical tested.

Q. In the preamble to those reports do they define the standards for judging whether a substance is carcinogenic or not, set forth criteria for that?

A. Yes.

Q. Let me hand you what has been marked as Plaintiff's Trial Exhibit 70. It has been previously furnished to opposing counsel. Do you recognize that

document?

A. I do.

Q. And what is that document?

A. It's Page 2 of a typical National Toxicology practice, bioassay report.

Q. Does it in the face of that document contain the standards for judging the evidence on carcinogenecity of chemicals?

A. Yes, it does.

MR. BRALY: With the Court's permission, I will move the admission of the document. I have an enlargement.

THE COURT: Any objection?

MR. JENNINGS: No objection, Your Honor.

THE COURT: Plaintiff's 70 will be admitted.

Q. (BY MR. BRALY) Doctor Lijinsky, let me call your attention to what has been marked as Exhibit 70-A. Do you recognize that portion of the document?

A. I do.

Q. Would you read to the jury that portion that begins "clear evidence of carcinogenicity."

A. "Clear evidence of carcinogenecity is demonstrated by studies that are interpreted as showing chemically related increased incidence of malignant neoplasms, studies that exhibit a

substantially increased incidence of benign neoplasms, or studies that exhibit an increased incidence of a combination of malignant and benign neoplasms where each increases with dose."

Q. Doctor Lijinsky, are you familiar with a study done by Doctors Hoffmann and Hecht where they painted the mouths of laboratory animals with NNN and NNK?

A. Yes.

Q. Before I come back to that, do you know Doctor Hoffmann and Hecht?

A. Very well.

Q. Within the world of scientists that study nitrosamines, what part of the world do they have their particular expertise in?

A. They are specialists in the study of tobacco carcinogenesis.

Q. Are there any other scientists that you know of in the world that know as much about that particular subject as those two gentlemen?

MR. JENNINGS: If the Court please, we object to that.

THE COURT: Overruled.

A. No. Not as far as I know.

Q. (BY MR. BRALY) Not anybody else that knows

any more about it?

A. Not anybody else.

Q. Now, back to this experiment. Have you read their report or discussions, experiment with this mouth painting with NNN and NNK?

A. Yes.

Q. I understand that's not your particular specialty area, the tobacco portion of it. You study nitrosamines in general; is that correct?

A. Right. I read a great deal of literature on nitrosamines, as much as I can get my hands on.

Q. By the standard of the National Toxicological Program, are the nitrosamines NNN and NNK carcinogenic to the oral cavity of those laboratory animals?

A. Yes, in my opinion.

Q. Doctor, what are mutagens?

A. Mutagens are agents that change the genetic constitution of cells.

Q. And have there been any -- let me ask you this question. What is, within the realm of our understanding of carcinogenesis, has there been any connection between agents that are mutagenic agents that are carcinogenic that have been suggested in the literature?

A. Yes. Most people believe or some people have some experts, authorities have stated that 90 percent or thereabouts of carcinogens are also mutagens.

Q. Does this depend a little bit on the particular class of carcinogens that are involved as, --

A. Yes.

Q. -- for instance, a class of hormonally driven carcinogens as opposed to the class of nitrosamines?

A. Yes.

Q. Does this vary between class?

A. Yes, this is -- that was a comprehensive number, but there are -- there are groups of carcinogens, for example, polycyclic -- chloride hydrocarbons that are almost all noh -- not mutagenic. They are carcinogenic, but not mutagenic, and most steroid hormones are not -- are carcinogenic but not mutagenic. But most carcinogenic nitrosamines are also mutagenic.

Q. Has there been any test that has been developed that is a relatively inexpensive test as to whether a chemical causes mutations?

A. Yes.

Q. What is that test called?

A. It is called the -- for short it is called Ames test, because it was developed by Doctor Bruce Ames at Berkeley, but it is properly called the Salmonella typhimurium histidine reversion assay.

Q. Have you caused Ames tests to be performed from time to time in connection with your work?

A. For mutagenesis?

Q. Yes.

A. Yes, I have. In fact, I had a laboratory as part of my program at one time -- it was separated from, set up separately -- that was entirely devoted to mutagenicity tests and bacteria.

Q. Are these expensive tests to run?

A. No, it is cheap.

Q. Approximately how much does it cost to get one run?

A. I would say between 2- and $600, $200 and $600 per compound.

Q. Can substances like snuff be tested on an Ames test?

A. Yes, they can be.

Q. When did the Ames test become available?

A. About 1973 in its fully-developed form.

Q. So by the middle of the 1970's could a

company like the U.S. Tobacco Company have caused an Ames test to be run on its product?

A. Yes.

Q. Doctor, let's talk about nitrosamines in particular for a few minutes. You may have, I believe, heard the jury last week listened to Doctor Hoffmann and Doctor Hecht by videotape, and they are pleased to have a live witness this morning.

But, in general, what is there about nitrosamines that makes them significant?

A. Their main characteristic is that they cause cancer.

Q. If it wasn't for that particular characteristic of this class of chemicals, would they be of any interest, any particular interest to science?

A. They would be of some interest, but they -- until they were discovered to be carcinogenic, they were a real back order of chemistry. I mean there were no -- no large studies devoted to chemistry of nitrosamines.

Q. Approximately when were they first discovered to be carcinogenic?

A. 1956 was the first published report.

Q. Now, have you personally tested a number of

these nitrosamines?

A. More than a hundred sixty of them.

Q. Are you familiar with a scientist by the name of -- I believe it is Preussmann?

A. Preussmann.

Q. Preussmann?

A. Yes. He is a good friend of mine.

Q. Has he reviewed the literature on this subject?

A. Yes. He published a review in 19 -- the end of 1984, and it was a chapter, a very long chapter in a book entitled "Chemical Carcinogens," and this chapter was called "N-Nitrosocompounds," which is the proper chemical name of nitrosamines, more specific chemical name.

Q. Doctor Lijinsky, have you prepared an exhibit that represents the status of the review of those compounds by Preussmann and by yourself?

A. Yes.

Q. Is this that exhibit, sir?

A. Yes, it is.

Q. Can you see it from where you are?

A. I can.

Q. If I may, I will just hold it here.

A. That has been identified as Plaintiff's

Trial Exhibit No. 19.

Now, with respect to those that have been reviewed by Doctor Preussmann, approximately how many of these compounds have been tested for their carcinogenicity?

A. 303.

Q. And approximately, if you will, what percentage of those have been shown to be carcinogenic?

A. 86 percent.

Q. When we say tested, are we talking about a full-blown laboratory test where these are given to laboratory animals and control animals, that sort of thing?

A. Yes, the tests that were reviewed by Preussmann were all chronic toxicity tests, that is long-term tests where animals were treated with the compound -- with the compound, with the nitrosamine for a good part of their lifetime.

Q. This portion down here at the bottom, I take it Lijinsky is referring to yourself?

A. Yes.

Q. And it shows 157 as being the number of compounds that you personally have tested?

A. At that time. I have tested a number since

then, which probably figures up to maybe a hundred sixty-five or so.

Q. And out of that 157, how many of them are shown to cause cancer?

A. It was 136 or 87 percent.

MR. BRALY: Your Honor, I move the admission of Plaintiff's Exhibit 19, and we will provide a smaller copy for the record.

MR. JENNINGS: We have no objection, Your Honor.

THE COURT: Plaintiff's 19 will be admitted.

Q. (BY MR. BRALY) Doctor, in the world of science as it relates to chemical carcinogens, what is meant by the expression "broadly-acting chemical carcinogens"?

A. It means a group of carcinogens that cause cancer in many different species and many different organs of those species.

Q. Are there other carcinogens that are not broadly-acting, beside --

A. Yes. Yes, there are.

Q. What is the significance of a class of chemicals being designated or categorized as being broadly-acting carcinogens?

A. It suggests or it indicates that these

compounds, the carcinogens that are in this class, in this category are likely to be -- to produce cancer in a great variety of organs, and that the risk to humans would be commensurately greater.

Q. Doctor, have you caused to be prepared an exhibit that lists a number of different carcinogens that have been tested and are understood by science?

A. Yes.

Q. Does it in some way prepare that by the appropriate dose it takes to induce cancer?

A. Yes.

MR. BRALY: Your Honor, I am going to place on the board what has been marked Plaintiff's Exhibit 18. Counsel has got a copy of it.

THE COURT: Any objection to Plaintiff's 18?

MR. JENNINGS: No, Your Honor.

THE COURT: Plaintiff's 18 will be admitted.

Q. (BY MR. BRALY) Doctor Lijinsky, let me call your attention to that exhibit. Did you prepare that and furnish it to me so I could get it enlarged for this trial?

A. I did. And they are in fact my calculations. They are not derived from anybody else's suggestion. I made the calculations myself.

Q. One moment, Doctor. Doctor, the one at the

top, what is that?

A. Aflatoxin is a carcinogen produced by fungus. Aspergillus is the name of the organism, and it's a common contaminant of food, so moldy food often contains this substance aflatoxin.

Q. Is it considered to be a potent carcinogen?

A. Indeed, yes.

Q. Is it broadly acting?

A. No.

Q. Can you give us some examples of what you mean by that it is not broadly active?

A. It is a very, very potent carcinogen. Was, in fact, considered the most important carcinogen in liver.

Q. It's liver tumor in rats?

A. In mice it doesn't give any tumors at all of any type. In monkeys it required enormous doses to produce tumors and over a very long period of time, and in hamsters it is also a very weak carcinogen, so it is not a broadly acting carcinogen. It is very narrowly acting.

Q. Doctor, the next two on your list, would you read those names, please?

A. Nitrosodimethylamine and nitrosomorpholine.

Q. What class do they represent?

A. They are nitrosamines.
Q. Could I group them to go as N-nitrosocompounds?
A. Yes.
Q. Now, compare their characteristics in terms of being broadly-acting carcinogens with those of aflatoxin.
A. Oh, they are enormously more broadly active. Nitrosomorpholine, for example, which is just a typical nitrosamine, induces tumors of the nasal cavity, lung, tongue, trachea, which is the tube leading from the mouth to the lungs, and the esophagus, so it produces tumors of several different organs in several different species. It is not only active in rats, it produces tumors in hamsters and mice and guinea pigs, and I'm not sure which other species it is being tested in.
Q. Doctor, as a class, based on your knowledge and understanding, approximately how many different species have nitrosamines been tested in to see if they will get cancer as a result of exposure to nitrosamines?
A. I think the present number is 45, but new species are added as scientists become interested in examining the carcinogenic effects of nitrosamines in

other species. They might add a species that happens to interest them.

Q. Does that include primates?

A. Oh, yes.

Q. Monkeys?

A. It includes monkeys of several kinds.

Q. Have any of those species to your knowledge shown themselves not to be susceptible to getting cancer as a result of exposure to various different kinds of nitrosamines?

A. None. No species has been found which is resistant to nitrosamine carcinogenesis.

Q. Doctor Lijinsky, if somebody were to deliberately go out and give nitrosamines to human beings, do you know of any reason why the human species would be exempt from that pattern?

MR. JENNINGS: If the Court please.

A. Well, --

MR. JENNINGS: We object as speculation by the witness.

THE COURT: Overruled.

Q. (BY MR. BRALY) You may answer.

A. I don't know of anybody who has done such an experiment, but I have no doubt that humans would be susceptible.

Q. Let's talk about some of these here.

A. What is Benzo(a)pyrene?

A. Benzo(a)pyrene is a product of pyrolysis or combustion of organic countersubstances, and it is a potent carcinogen for the skin.

Q. Now, the doses that you have got listed over there, how do they relate to the kinds of doses that are involved with nitrosamines?

A. Well, you you mean the ones below.

Q. Well, on the right-hand side, you have got like 50 to 100 milligrams per kilogram?

A. Yes. Well, that's -- I said Benzo(a)pyrene is potent carcinogen for the skin. It is not a terribly potent carcinogen for the hamster lung in which it also induces cancer. That implies that it is at least, Benzo(a)pyrene is at least 20 or 30 times less potent as a carcinogen than the nitrosocompounds.

Q. What about vinyl chloride? What is the situation with it?

A. That is much less potent even than Benzo(a)pyrene. Vinyl chloride is a substance that is known to induce cancer in humans, and it's generally accepted as a human carcinogen, and it produces tumor in the rat's liver, but only at doses

of several hundred or even a thousand times higher than those of nitrosamines.

Q. The next three items on the list, the 2-n-a-p- -- Pronounced?

A. 2-Naphthylamine.

Q. And the next one?

A. Benzidine.

Q. And the last one at the bottom?

A. The last was Azo-dyes which is a group of compounds. I couldn't give the specific one, but they are -- I just decided to include them as a class. Azo-dyes have a very narrow spectrum of carcinogenic activity. They produce tumors of the liver in rats but not in mice.

Q. Are the two above it, the 2-Naphthylamine and the benzidine, are they related to each other?

A. Yes, they both belong to the class called aromatic amines. They are --

Q. Would you say that again?

A. They are both in the class of aromatic amines.

Q. Spell that.

A. A-r-o-m-a-t-i-c a-m-i-n-e-s, aromatic amines. And these are substances that are involved in making dyes. They were suspected of being

carcinogens for humans as long as 60 or 70 years.

Q. Are they known to cause cancer in humans?

A. Yes.

Q. How do you compare their potency with those of nitrosamines?

A. Oh, they are thousands of times less potent.

Q. Now, is it legal at the present time to manufacture 2-Naphthylamine?

A. I don't think it is legal in most countries to make 2-Naphthylamine.

Q. And why is that?

A. Because it is such a dangerous potent carcinogen.

Q. It did previously have some industrial purpose?

A. Yes, it was -- well, benzidine was used in fact in test strips for the blood, and that use of it has been banned now.

Q. Now, Doctor, let's talk a little bit about our understanding of the causes of cancer that are induced by chemicals. Do we from the history in this field, are there any examples of our understanding of chemically-caused cancer that date back to the 1700s?

A. Yes.

Q. Can you give the jury an example of that.

A. The -- almost the first, not quite the first, the first was cancer of the nose induced by snuff in fact in 1763. I think there was a report of that, but the most -- the one that is best remembered is skin cancer of the scrotum of young men who were chimney sweeps.

From an early age they were sent up chimneys as little boys to sweep out the chimneys. The chimneys in big houses there are large, and they swept out the chimneys and they were exposed to a lot of soot, and the surgeon in London in the 1770's observed several of his patients, several of these young men he saw have this particular cancer that he never saw in anybody else.

He apparently asked people about their history, what they did, and he found that this particular type of cancer was -- was found only in the people who were chimney sweeps, and he called it chimney sweeps' cancer.

Q. And do we know what it was in the soot from the chimneys that was causing this cancer?

A. Yes.

Q. What was it?

A. It was polycyclic hydrocarbons, cyclic aromatic hydrocarbons that I mentioned I worked on

when I first started research on cancer.

Q. Did these young men that were exposed to this chemical carcinogen, did they get cancer at the end of their lives or while they were still very young?

A. Oh, no, I think in the -- in their teens.

Q. Now, all right. So is that an example from the 1700's of a chemically caused cancer?

A. Yes, it is.

Q. Do we have an example from the 1800's of chemically induced cancer that we know about?

A. Yes.

Q. What would that be?

A. I think the aromatic amines are good -- are a good example.

Q. Could you explain that a little bit, please.

A. There was a physician in Ruhr, Germany, who noticed that some of his patients had bladder cancer, which he saw very rarely in the general population. He found these people all worked in dye factories, and it was because they worked with aniline dyes. He called it aniline cancer. We now know that the cause of those cancers -- those bladder cancers were not aniline but other aromatic amines that belong to the same class as aniline.

Q. Doctor, in the 1770's what was the name of the British surgeon that was related to the chimney sweep cancer?

A. Percival Potts.

Q. And so when Doctor Potts discovered the cause of the chimney sweep cancer, did medical science then understand the exact biological mechanism that caused it, the cellular cancer?

A. No. In fact, there were no signs of organic chemistry at that time. It would have had no meaning to question what type of chemical was involved in this, because there were no signs of organic chemistry.

Q. Doctor, you today, do scientists such as yourself understand the exact mechanism by which cells in the human body become malignant?

A. No, not in any case.

Q. With respect to the example of the aromatic amines during the 1800's, did scientists understand the exact biological mechanism then?

A. No, we know -- we understand a few of the steps in what we call activation of those chemicals, but we do not know how they cause cancer.

Q. Are the causative effects of chimney sweep cancer and the causative effect of the dye with

cancers and in the dye workers, are those well-accepted causal relationships in the field of chemical carcinogenesis?

A. Yes.

Q. Doctor, there has been some mention in the testimony last week that certain nitrosamines were organ specific.

A. Yes.

Q. Can you tell the jury a little bit about that and explain it and help them understand what is going on with respect to those nitrosamines.

A. Organ specificity describes the tendency or the characteristic of a nitrosamine of a particular chemical structure to have as its target in a particular species one organ or one of several organs.

For example, some nitrosamines have as their target organ the liver or the lung, and they cause cancer in that organ independent of how they are given to the animal. In other words, they can be given by injection or they can be inhaled or they can be put on the skin, and they still find their way to the liver and produce the liver tumors or lung tumors, whatever it is.

On the other hand, there are some

nitrosamines that also have a local effect. That is, they produce tumors where they are put, where they are first applied.

Q. Doctor, with respect to this target organ situation, can those target organs vary from one animal to the other?

A. Yes, they can.

Q. So just because the target organ in one animal is the esophagus, does it tell you for sure which target organ that it is going to be in the next animal?

A. No.

Q. Now, what is the evidence or can you describe briefly for us the evidence that these nitrosamines also act as contact carcinogens?

A. There's one chemical, -- I'm afraid I'll have to tell you its name -- it is nitrosomethylamine, which I was interested in.

Q. Excuse me. Is that a nitrosamine?

A. That is a nitrosamine.

Q. Why didn't you refer to it as just nitrosamine?

A. Right. When I say "N-nitroso," it means it is a nitrosamine. That compound interested me because it was a member of a big series of

nitrosamines that I study. It was originally reported as not carcinogenic, because I don't think it was probably -- because it wasn't tested properly in the first case.

I tested this in two ways. I gave it by injection, by syringe, into the rats, and in that case it produced liver tumors and lung tumors. When I gave it in drinking water, it produced liver tumors and lung tumors but also tumors of the esophagus, because in that case of the drinking water, the esophagus was buried with the compound as the solution went down the throat into the stomach. And in that case I got esophageal tumors, quite a lot of them, in fact, a common tumor in those animals. That led me to believe that although there might be what we call a systemic effect, that is also -- that was also a local effect of the substance which led to the production of the esophageal tumors.

Q. Doctor, in conducting experiments with nitrosamines, is there a difference between the effect of administering, say, single large doses as opposed to repeated but smaller doses of those chemicals?

A. Yes.

Q. Would you describe to the jury the

significance of the difference.

A. The single large doses very seldom give rise to tumors. Sometimes a few tumors develop and the animals survive single large doses. Single large doses tend to, if they are high enough, lead to death of the animals because of toxicity to the cells, killing so many cells. On the other hand, small frequent doses tend to be much more effective in inducing tumors, and, in fact, you can see an effect of small -- of frequent doses down to very low levels, very low dose levels.

Q. Doctor, there have been a number of exhibits taken from the literature reflecting different levels of nitrosamines. I want to stop for a minute and take a few minutes that involve different units to express these, and I want to make sure that this is clear to the jury so --

I don't find the right one. Let me start with this one.

A. This I will need my glasses.

Q. Here they are right here, I'm sorry, precisely the ones I wanted.

Doctor, the chart up here, for instance, reflects --

THE COURT: Excuse me.

Q. -- the level of nitrosamines?

THE COURT: What is the exhibit you are referring to?

MR. BRALY: Excuse me. The trial exhibit number, Trial Exhibit 229.

THE COURT: Is it in evidence?

MR. BRALY: Yes.

Q. (BY MR. BRALY) I call your attention to the top table up here. It expresses the nitrosamines in snuff in these units right here. Would you describe those, please, if you can.

A. The units are micrograms per kilogram.

Q. All right.

A. That is millionths of a gram per kilogram of snuff.

Q. Can you relate that to something that they heard repeatedly called parts per billion?

A. Yes. One microgram per kilogram is one part per billion.

Q. So these units would be expressed in parts per billion?

A. Yes.

Q. And is that the same for the units in this chart down here?

A. Those are in parts per billion, yes.

Q. Now, sir, going to an earlier exhibit, Trial Exhibit 122, it shows up here that tobacco-specific N-nitrosamines and it's got ppm right there. What does that mean?

A. That means parts per million.

Q. So what would you have to do to, for instance, convert the levels of NNN into parts per billion?

A. Multiply them by a thousand. In other words, that 39 would become 39,000.

Q. And the 26.5?

A. Would become 26,500.

Q. And that would be parts per billion?

A. Parts per billion.

Q. Is ppb an adequate abbreviation?

A. Yes.

Q. That would be true all the way through?

A. Yes.

Q. Is that correct?

I believe there is one further exhibit.

Let me call your attention to what has been marked as Plaintiff's Trial Exhibit No. 121. Again, the units up here in micrograms per gram?

A. That's parts per million.

Q. That is the same as parts per million?

A. Yes.

Q. All right. And this number right here, can you translate that number into parts per billion?

A. Yes, it would be 88,600.

Q. Parts per billion?

A. Parts per billion.

Q. Okay. And again just by multiplying that by a thousand, you --

A. Yes.

Q. -- convert it into parts per billion; is that correct?

A. Yes.

Q. Now, these units down here, right there, they say ppb. What does that mean?

A. They are in parts per billion.

Q. So they are already in parts per billion?

A. Yes.

Q. Doctor, would you describe, if you can, a typical one of these experiments that you do in the laboratory with nitrosamines, try to describe how you conduct it, a little about how it's done.

A. How I do it?

Q. Yes, how you do it.

A. I select a group of animals, I order a group of animals from the animal production area. Our

animals are bred under very carefully-controlled conditions so they are all healthy, and we could normally expect them all, if untreated, to live about two-and-a-half to three years.

And we get a group of these at random, varying in size, from 20 to a hundred, and I make up a solution of the particular nitrosamine I am going to test as a stock solution. It is then diluted, usually into drinking water in carefully measured amounts, and then it is supplied to the animals in their drinking water bottles.

And that treatment goes on for a prescribed length of time, which I determine based on previous experience, and then we terminate the treatment and let the animals die. They usually die of tumors induced by the carcinogen.

Q. Doctor, at what age do you usually start the treatment of these animals?

A. Six or seven weeks old.

Q. Are these mature animals by that time in their life span?

A. They are not -- no, they are not capable of reproduction at that age, but they will be within a month.

Q. Now, --

A. They are not babies.

Q. And approximately how long do you let them have these chemicals in their drinking water?

A. It varies. If I'm using one of the carcinogenic nitrosamines at a high dose, I usually do treat them for six months, but the treatments can be as long as two years at low doses.

Q. Now, what is the significance of age in its relation to the cause of these chemically-induced cancers?

A. We found -- and this is an experience I have had which confirms what is already in the literature -- that animals treated at a young age develop their tumors earlier than animals that are treated at later ages.

Q. Doctor, is old age a prerequisite of getting cancer?

A. I beg your pardon. I didn't quite get the question, Mr. Braly.

Q. What I am trying to get to, is old age something -- do you have to be old in order to get cancer?

A. People usually develop cancer in old age, in my opinion, or at least after middle age because the doses of carcinogen to which they are normally

exposed are small, and it takes time to accumulate the dose, except in the case of people who use tobacco.

Q. Are you telling us that it is not because they are old but just because they have accumulated sufficient doses that they are getting these cancers?

A. Yes.

Q. Has that same phenomenon been shown in laboratory animals?

A. Yes.

Q. Can you describe a little bit the evidence that supports that that you are aware of?

A. I will describe an experiment that I did recently. I took one group of animals, as I said, from the animal house, 20 or 24 animals, I don't remember exactly whether it was 20 or 24, and at the age of 7 weeks I gave them a certain treatment with a chemical -- with a carcinogenic nitrosamine called nitrosomorpholine, in fact, the one that was on the chart. I took an additional group of animals at the same time and I kept them until they were 60 weeks old, untreated, just kept them in the animal house, and then I gave them exactly the same treatment that I gave the younger animals, the group of 20 animals that were 60 weeks old, gave them exactly the same

treatment. It took the older animals two or three times as long to develop tumors from which they died than it took the younger animals. And that was convincing evidence to me that the older animals are less responsive to the same dose of carcinogen than the younger animals.

Q. Doctor, with respect to the life span of these animals, the animals you described only live for a couple of years.

A. Yes, sir.

Q. How long typically does it take for these tumors to appear in animals that only live for two or three years?

A. They usually appear between one and two years of age.

Q. What happens if you give the same body weight dose of these chemicals to a laboratory animal that lives longer than that? How long does it take them? Does it take them nearly all their lifetime, or do they get it in the same length of time?

A. No, it still takes about two years.

Q. Have there been a number of experiments that have confirmed this?

A. Yes. There's -- the most widely tested nitrosamine is a substance called

nitrosodimethylamine, or NDEA, as we call it -- as we abbreviate it. That compound has been given to monkeys, to cats, to frogs, to snakes, and to chickens, as well as other -- as well as other species, but these happen to have a much longer life span than rats. In each case the tumors developed within about two years, as it did in rats, as they did in rats. They were usually liver tumors.

Now, the python, which was the snake that was tested by Mr. Schmahl in Germany, lives -- has a life span between 30 and a hundred years, no one knows exactly. The cat, cats were another species that were tested. Cats live typically 15 to 20 years. Chickens live approximately 15 years. Guinea pigs live six to eight years, but in each case the tumors appeared two years after the -- after the treatment with approximately the same dose per unit body weight as the rats received.

So I think this convinces me that the time of appearance of tumors is related not to the life span of the animal but to the dose the animal receives of the carcinogen.

Q. Doctor, what about dose in laboratory animals. Everybody has heard or read stories in the newspaper about very large doses of chemicals given

in laboratory experiments. They have criticized experiments for that reason. In the experiments that you have done with nitrosamines, can you compare that with these other kinds like, for instance, the saccharine experiments?

A. Oh, the doses I used typically for my nitrosamine experiments are of the order of maybe ten to a hundred parts per million, usually, of the nitrosamine in drinking water. They are thousands of times lower than than the dose, saccharine, that was needed to produce cancer, so the doses of nitrosamines are not very high. They are not excessive.

Q. With respect to the doses of nitrosamines that have been given to laboratory animals, are these comparable to what humans can be exposed to, for instance, from snuff-dipping?

A. Yes, they are very comparable.

Q. Is that on a, for instance, a body weight basis?

A. Yes, on a body weight basis on an absolute basis.

Q. In connection with your work on nitrosamines, have you calculated a total dose per kilogram of body weight that in your opinion would be

sufficient to induce cancers?

A. Yes.

Q. Approximately how much was that?

A. I think the lowest dose that was -- that I would consider carcinogenic dose, that is it gave rise to a number of induced tumors in the animals, was about 7 micrograms per kilogram body weight per day.

Q. And how long did they get that?

A. In that particular experiment, for two years.

Q. Have you got notes or anything there? Can you check and see --

A. Yes, I'm sorry.

Q. -- what the total lifetime dose was?

A. The total lifetime dose of those animals was about 13 or 14 milligrams per kilogram, I think, of nitrosomorpholine. Sorry, 7 milligrams per kilogram per body weight in two years.

Q. 7 milligrams?

A. 7 milligrams per kilogram.

Q. Now, I brought a salt shaker with me today. Would you, sir, -- what was the number that I just said? What was the number that I just mentioned? 7?

A. 7 milligrams per kilogram.

Q. Is that the right number?

A. Yes.

Q. Is that your experience with nitrosomorpholine?

A. Yes.

Q. Can you take that salt shaker and show the jury what a milligram is or something that approximates a milligram?

A. It is hard to do, because it is actually about two or three grains. I am afraid I can't shake out two or three grains. That is several milligrams, the amount I am showing you. It is about two or three grains, hard to tell.

Q. Doctor, have you made any calculations to see what a snuff dipper might get in the way of a dose of nitrosamines from dipping Copenhagen Snuff over a period of about six years?

A. Yes. It is -- excuse me a second. About 16.6 milligrams per kilogram body weight.

Q. Was that based on Copenhagen Snuff?

A. Yes, it is based on the consumption of about two-thirds of a can a day of snuff.

Q. Did you use these values from this 1982 report on the levels of nitrosamines in Copenhagen?

A. Yes. Yes, I did.

Q. And what was the lifetime dose?

A. 16.6 milligrams per kilogram of body weight.

Q. What weight of a person did you use?

A. A hundred -- I think 130 pounds.

Q. Pounds?

A. Approximately.

Q. 60 kilos?

A. 60 kilos, yes.

Q. Doctor, at low doses of nitrosamines -- let me ask you one other question about the data.

Are all of these nitrosamines known to be carcinogenic, or is there one of these that is not known to be carcinogenic?

A. All of them are carcinogenic except the one labeled NAT, which is nitrosoanatabine, which is usually considered not to be carcinogenic.

Q. Did you exclude it from your calculation?

A. I did.

Q. What about NAB?

A. I didn't include that either. That's -- I excluded NAB, also, because that is a much weaker carcinogen than any of the others.

Q. Included or excluded it?

A. I excluded.

Q. So excluding those two, you still came up

with 16.6 milligrams per kilogram of body weight?

A. Yes.

Q. Now, Doctor, among those nitrosamines is included the nitrosamine that has been referred to as NNN?

A. Yes.

Q. And also NNK?

A. NNK.

Q. And also NMOR?

A. Yes.

Q. Nitrosomorpholine?

A. Yes.

Q. In the experiment done by Doctor Hoffmann and Hecht where they painted the mouth, was that done with NNN and NNK?

A. Yes, it was.

Q. Have you done experiments with nitrosomorpholine?

A. Yes.

Q. What was the purpose of that experiment that you did with nitrosomorpholine?

A. It was to establish a dose response relationship between the dose the animals received and the instances of cancer among them. This type of dose response experiment is usually done in

carcinogenesis for the purpose of risk assessment, that is for trying to measure the potential risks to people who are exposed to that particular carcinogen.

I had a large group of animals in this experiment, more than 600 animals divided into groups, each of which -- each group of which was given a different dose or the same dose for a different length of time, a year or two years, and so we could relate the number of tumors that appeared and the number of animals with tumors and the types of tumors that were induced to the strength of the dose. And we, from a large portion of the animals, developed tumors as a consequence of the treatment with nitrosomorpholine.

Q. Doctor, at the low dose levels in this dose response study, did you observe any cancers of the oral cavity?

A. Yes.

Q. And were there any other particular subsites that were caused, which cancer occurred as a result of exposure to nitrosomorpholine?

A. They were overwhelmingly in the tongue.

Q. Were they benign tumors?

A. They were both benign and malignant.

Q. And the malignant portion of the tumors, what kind of malignant tumors were they?

A. They were squamous cell carcinomas.

Q. Of the tongue?

A. Of the tongue.

Q. At the lowest dose levels?

A. Yes.

Q. Is that same nitrosamine found in snuff?

A. This is one of the nitrosamines found in snuff.

Q. Doctor, in the experiments that you do, do all the animals always get cancer?

A. No. Only at the very highest doses do all the animals get tumors in such an experiment.

Q. At the very, very low doses?

A. At the very low doses, a portion of the animals get tumors.

Q. But not all of them?

A. Not all of them.

Q. Why don't the others get cancer?

A. Because in rats, as in all other animals, there's a large biological variation in the way in which the animal deals with foreign chemicals.

Q. Is this a natural phenomena?

A. Natural?

A. Yes, it occurs in all species, including humans.

Q. Doctor, are there other sources of exposures to nitrosamines that everybody in this courtroom in the course of going through their daily lives comes in contact with?

A. Yes.

Q. Can you give us some examples?

A. One example is cured meats. Bacon, sausage, ham, corned beef and so on, all have some nitrosamines in them because they are cured with nitrite, and the nitrite is the source of the nitrosamine. Beer is another example, whiskey, distilled spirits in all cases, of all types.

Q. Doctor, on a daily basis have there been any estimates that you consider to be reasonably accurate as to what the exposure from other sources of nitrosamines is besides tobacco and tobacco smoke?

A. It's very small compared -- by comparison. It probably represents no more than an average of one microgram per day per person.

Q. Now, we have been talking about milligrams up here; is that correct?

A. Yes.

Q. And how much smaller than a milligram is a

microgram?

A. It is one thousandth of a milligram.

Q. That comes from the collection of other exposures to which people might come in contact?

A. Yes.

Q. Now, have you run a calculation to see how many micrograms of nitrosamines that a person like Sean Marsee who used something like two-thirds of a can of snuff per day would receive from his snuff-dipping?

A. Per day?

Q. Yes, sir.

A. Yes, I think I did that calculation. Approximately 476 micrograms per day.

Q. So would that -- do I interpret that correctly as being 470 times larger than all other exposures to nitrosamines put together?

A. Yes.

Q. Now, can nitrosamines be formed inside the human body?

A. Yes.

Q. How much do we know about that subject?

A. We know something about it. Their experiments are difficult to do because we don't usually experiment on people particularly. We don't

want to give them known carcinogens, so the experiments have been done have used -- have looked for the formation of noncarcinogenic nitrosamines, a few nitrosamines are not carcinogens, and they involve giving a person an amine and nitrite and measuring how much nitrosamine is formed.

These experiments are not very precise, and the estimate is that the exposure of the average person will be about the same as from external nitrosamines, that is, about a microgram per day per person or thereabouts. It could vary quite a bit from one person to another, depending on what they are exposed to and also upon their biological constitution, but it probably isn't more than ten times that in the worst case.

Q. If you compare even the combination of those worst-case situations to the exposure that you just described from snuff-dipping, how do they compare?

A. It would still be only about a 50th of what Sean was exposed to in the form of nitrosamines in snuff.

Q. Now, Doctor, just because there was that many nitrosamines in the snuff, that doesn't mean that Sean Marsee consumed all of those, does it? It doesn't mean they all got into his body and stayed

there, does it?

A. No, not necessarily.

Q. It would be like some snuff dippers do, expectorate from time to time, that he might have gotten rid of some of them; is that correct?

A. Yes.

Q. Some of them may have remained in the quid when he would spit out the used tobacco.

A. Yes.

Q. Are you aware of any research that shows the presence of these nitrosamines in saliva?

A. Yes, I am.

Q. Is there a wide natural variation in the levels of these nitrosamines in saliva as a result of individual variations in the reaction to snuff-dipping?

A. Well, in the experiment that I have seen published, there was a very wide variation.

Q. Does that surprise you?

A. No.

Q. Is that something that you would expect based on your experience in dealing with different individuals among different species?

A. Yes, it is.

Q. Doctor, in comparing the relative potency,

how do the nitrosamines like NNN and NNK and NDMA compare in their relative potencies?

A. They are all very comparable. They are similar in potency.

Q. Have you looked at the bar chart that was prepared by Doctor Hecht to demonstrate this phenomenon?

A. Yes.

Q. Your opinion in reviewing that matter, does that present useful information to understand the relationship between the doses that Sean Marsee received and that are known to cause cancer in laboratory animals?

A. Very much so.

MR. BRALY: Your Honor, at this time we would reurge the admission of that bar chart exhibit that was first identified by Doctor Hecht in his deposition.

THE COURT: Overruled at this time.

Q. (BY MR. BRALY) Doctor, with respect to nitrosomorpholine, when was it first shown to be carcinogenic?

A. I think about 1963 or -4.

Q. Was it ever the subject of a review by the International Agency for Research on Cancer?

A. Yes, it was.

Q. And did you participate in the working group that accomplished that review for the International Agency for the Research of Cancer?

A. Yes.

Q. Were you invited by the International Agency for Research on Cancer to participate for that purpose?

A. I was.

Q. Doctor Lijinsky, let me hand you what has been marked as Trial Exhibit 120. Do you recognize that volume, sir?

A. I do.

Q. I am at a slight disadvantage, because that is the only copy of that that I have, so I may need your cooperation a little bit. Before we get into the details of the volume, I would like to ask you a few questions about the IARC series in general. Those monographs, do they come out in a sequential series?

A. Yes.

Q. And what is the purpose of that series of reports?

A. They are to evaluate for the scientific community the potential risk of -- risk to humans of

exposure to carcinogens.

Q. are these reports made at or near the time or transmitted from information from scientists like yourselves that are working for the IARC?

A. Yes, they usually appear within six months of the holding of the meeting at which the matter is discussed.

Q. Are these documents kept and those reports kept and produced in the ordinary course of business of the International Agency for Research on Cancer?

A. Yes.

Q. And is it the regular practice of the International Agency for Research on Cancer to cause these monographs to be prepared and kept?

A. Yes, it is one of the most important functions.

Q. Doctor, in particular respect to that particular monograph, let me call your attention to, I believe, Page 275 of the document.

A. 275?

Q. Yes, sir.

A. Yes.

Q. Do you see there a portion that evaluates the effect of nitrosomorpholine?

A. Yes.

Q. Would you read that evaluation.

A. Yes. "Section 4.3, Evaluation. There is" in italics "sufficient evidence for a carcinogenic effect of N-nitrosomorpholine in several experimental animals species. Although no epidemiological data were available, N-nitrosomorpholine should be regarded for practical purposes as if it were carcinogenic to humans."

Q. Doctor, I don't want to take the Court's time and the jury's time, but if you went back into that portion of the volume, could you read the details of the various different experiments that were done to substantiate that conclusion?

A. Various experiments?

Q. Yes.

A. Animal experiments, yes.

Q. They are set forth in the volume?

A. Yes, they are.

Q. Doctor, is that a summation of the evaluation of those experiments?

A. Yes.

Q. Doctor, let me call your attention to, if you would, Page 284.

A. 284? Yes.

Q. That is a section that deals with

nitrosonornicotine?

A. Yes.

Q. Is that the same NNN that Doctor Hoffmann and Doctor Hecht have found in snuff?

A. Yes, it is.

Q. The same chemical?

A. Yes.

Q. Was that chemical also evaluated in that volume of the IARC?

A. Yes.

Q. Was that chemical known to be present in snuff in 1978?

A. No, -- it might have been suspected -- yes, it was certainly present in tobacco. I don't know whether snuff per se had been analyzed at that time. I had seen no reports of analysis of snuff for nitrosamines, but it was known to be present in tobacco.

Q. Tobacco is in snuff?

A. Yes. A devious answer, but --

Q. Let's straighten this out. I realize you said you are not a tobacco chemist.

A. I'm not.

Q. If I showed you this chart --

A. Yes.

Q. -- from 1974, called your attention to Skoal Bandits right there at 88,000 parts per billion, would that affect your opinion on whether --

A. Yes.

Q. -- that had been known in the literature?

A. Yes. I'm sorry. I didn't remember that that was as early as 1974. I do note that chart.

Q. How many of these did you say you tested, Doctor?

A. 165, maybe, including nitrosonornicotine.

Q. I will forgive you if you forgot that one.

Now, Doctor, with respect to this evaluation of nitrosonornicotine, that was the one that was present there at 88,000 parts per billion?

A. Yes.

Q. Would you read to the jury from this IARC report on summary of the evaluation.

A. "Section 4.3, Evaluation. "There is," again in italics, "sufficient evidence of a carcinogenic effect of N-nitrosonornicotine in several experimental animal species. Although no epidemiological data were available, N-nitrosonornicotine should be regarded for practical purposes as if it were carcinogenic to humans."

Q. Doctor, are all of this series of monographs

produced and maintained, recorded in the same fashion that you just described for No. 17?

A. Yes.

Q. Would that include this most recent one, Volume 37, dealing with tobacco habits other than smoking?

A. Yes.

Q. Doctor, I want to show you a document from the files of the tobacco company.

THE COURT: Ladies and gentlemen, while they are examining that, why don't we go ahead and take our midmorning recess. We will recess for 20 minutes. With my usual admonitions to you, you will be recessed for 20 minutes.

Everyone remain seated while the jury exits for 20 minutes.

Court will be in recess.

(A brief recess was here had.)

(The following proceedings were had OUT OF THE PRESENCE AND HEARING OF THE JURY.)

THE COURT: Be seated. There was an objection to the exhibit?

MR. JENNINGS: Yes, we want to take up our objection to the two proposed exhibits.

THE COURT: All right.

MR. BRALY: Before we do that, Your Honor, can I clarify the record on a couple of other exhibits that I was talking to him about?

Well, somebody, has called it to my attention that I had not been diligent in doing that. The IARC Volume 37 that I was referring to has been marked as Trial Exhibit 115, which I asked him if this was another example in the same series of monographs in connection with the business records.

THE COURT: You referred to Plaintiff's 120. Did you also -- which was the IARC study.

MR. BRALY: That was this particular version.

THE COURT: All right.

MR. BRALY: Okay. This is Volume 17, which has been marked as Plaintiff's Exhibit 120. This was the evaluation on some nitrosocompounds which included nitrosomorpholine and NNN. The other thing I wanted to refer to was this exhibit which I reurged the admission of an exhibit identified by Dr. Hecht in his exhibit, which has been marked as Exhibit 24 to Dr. Hecht's deposition and been marked for identification Plaintiff's Trial Exhibit No. 230 and reurge the admission of this exhibit based on this witness's testimony about the relative potency of

NDB, NDMA, NNN and NNK.

THE COURT: Do you want to respond? He is reurging, I believe it is Plaintiff -- What is the number it?

MR. BRALY: It is Plaintiff's Trial Exhibit 230.

MR. JENNINGS: I had understood the Court overruled that.

THE COURT: I did overrule it. This witness just testified that the nitrosamines, NNN and NNK.

MR. BRALY: NDMA.

THE COURT: NDMA were comparable to what?

MR. BRALY: They were comparable in potency. Is that correct?

THE WITNESS: Yes.

THE COURT: So I am asking what are your responses?

MR. JENNINGS: If the Court please, our position is the same as it was that is that the exhibit is misleading, in that it is comparing NNN and NNK with the other one, which is NDMA, I guess, and that it is misleading for other reasons, one of which is the calculation that Doctor Lijinsky made which I am going to cross examine him about when I get an opportunity.

THE COURT: I will hold that still in abbeyance. I have overruled it, but I will consider it after cross-examination.

Now, were you asking something in regard to Plaintiff's 115?

MR. BRALY: Yes. Yes, I am at this time, based on the foundation layed by this witness as to business records, would reurge the admission of Plaintiff's Exhibit 115, which is IARC Monograph Volume No. 37. We urge it for no other reasons under the business records compensation, I think he layed an appropriate foundation.

THE COURT: Does he represent the IARC?

MR. BRALY: He's worked for them before, Judge. He claimed that he had knowledge of their procedures, and I think he constitutes another qualified person. He helped produce that version and he's familiar with their procedures.

THE COURT: I will sustain the objection.

MR. JENNINGS: I was offering two more exhibits which he wanted to address, Your Honor.

THE COURT: All right. Clerk, what happened to 120.

120, is 120 also offered for the same reason? I just sustained in regard to 115.

MR. BRALY: 120 has already been admitted. This is the 1978 document; it was admitted on notice --

THE COURT: All right.

MR. BRALY: -- a long time ago.

MR. FINNEGAN: Let me see the 1972 document first, Mr. Braly.

MR BRALY: '72,'82?

MR. FINNEGAN: I'm sorry,'82.

THE CLERK: It has--

MR. BRALY: All right. This is an exhibit marked, Trial Exhibit No. 96. It came from the files of the tobacco company, and I am going to ask the witness questions about it. It refers to nitrosomorpholine. As the Court may note, there is in there what we may consider to be an admission, which is in view of the extreme toxicity of N-Nitrosomorpholine. It is to our own advantage to find out where the morpholine source is. We think that constitutes an admission of the serious problem of nitrosomorpholine, if the company recognizes it as being extremely toxic.

THE COURT: What do you want to inquire with regard to this.

MR. BRALY: I want to ask him if he agrees

with it, publish the document to the jury.

MR. JENNINGS: If the Court please, we object first because the document was not identified as one of the documents that would be offered in evidence. Secondly, we object to it because it's got the confidential stamp on it which the Court has previously ruled on.

MR. BRALY: I don't have any problems with the confidential part of it. As far as the other objection, Your Honor, this was one of the 80,000 pages of documents that we got the week before trial.

MR. FINNEGAN: We have looked at all of the list and the amended list, Mr. Braly, and we have not found that document listed on any of your exhibits.

MR. BRALY: You are absolutely right, it is not there. We didn't get a chance to find the thing until the trial had already started, before we could get through with the documents. Mr. Jennings you brought this filing to comply with the court order of March 15 discovery.

THE COURT: I don't see anything helpful by this witness for use of this document. I will sustain the objection right now to the confidential sticker until it is taken off. I see no reason other than that why -- well, bring it up later in the

trial. If it is not listed as an exhibit -- When were all the documents finally turned over?

MR. FINNEGAN: Your Honor, we complied with the June 9, -- with the May 9 order -- there was an order of the Court which ordered us to complete production by May the 9th, and we complied with that, Your Honor.

Now, I can't tell the Court whether this was produced on that day or two weeks earlier, but I know that production was completed on May the 9th.

THE COURT: Did I also have an order that you would have an extra date to exchange exhibits that were filed late like that?

MR. FINNEGAN: If the Court please, I recall that the Court said that they could submit a list of exhibits if they found anything in there that he wanted to use as an exhibit, but we have never received any supplemental list which has this document listed on it, Your Honor.

MR. BRALY: Your Honor, like I say, on the 9th, the last week they produced 80,000 pages of documents. Given the fact that they had filed on three different occasions to comply with the Court's discovery order in a timely fashion, we don't think it is unfair, as a matter of fact, we do think it

would be unfair to keep us from producing documents from this last group of documents.

We will try to put together a list, quite frankly, the Court is well aware we have been busy trying a lawsuit here, and you know, it is just -- it is all we can do. I don't think it is unfair to present this --

THE COURT: Right now I am going to sustain the objection for the confidential marker being on there. Take that off and I don't want -- that was one of the problems in going to trial that we had to deal with and that was the fact of discovery going on almost up to the moment of trial. Do you anticipate other documents that you have not advised them of?

MR. BRALY: Yes, Your Honor, we are still looking through some of these documents. Your Honor, there is 80,000 pages of them, and I will do everything we can to get a list of all of them right now that I can think of. There's about a dozen of them that I went through this last weekend that I intent to present, and I will do everything I can to get a supplemental list.

THE COURT: Why don't you give him a list of those and we will take this up more towards the end of the week, give them a chance -- give them a list

of what you have got right now and then if you feel like you are prejudiced by this, you can raise that. Right now, just remove the confidential sticker on that, you don't need this witness in regard to that.

MR. BRALY: I just wanted to ask the witness if he agreed with their company's characterization.

THE COURT: You can ask him whether he agrees that it is extremely toxic without going into that document. I think you already have. So I will sustain the objection right now.

Now, what else, what is the other one?

MR. BRALY: Note our offer of proof on the document, Your Honor, we think it is integral to this person's testimony.

MR. JENNINGS: This document, if the Court please, is dated July 18, 1984, has no relevance to this lawsuit.

MR. BRALY: Is that the extent of the objection?

MR. JENNINGS: That's my objection.

MR. BRALY: Your Honor, this document represents a statement of fact by the company, and the statement of fact by the company in our opinion constitutes an admission. It doesn't make any difference when it happened, the company in this

document states that these nitrosamines that are found in snuff are found in "high concentrations." This is an admission by the company that these are high levels.

THE COURT: What is VNA.

MR. BRALY: Volatile nitrosamines, that refers to this right here, which are four of them that are found in snuff, including one of them that this man has testified to, nitrosomorpholine. It also constitutes an admission that NMOR is a relative important potent animal carcinogen. It also constitutes a statement by the company that these are the highest levels of carcinogenic nitrosamines reported in a consumer product that is taken into the body.

Also we think this document is relevant, particularly relevant to this witness's testimony.

THE COURT: I will overrule the objection to that. I think it will be relative on the issue of causation.

MR. JENNINGS: Your Honor, we have one other problem. The Court will probably recall that we were ordered to furnish certain information with regard to compensation that people who were listed as witnesses had received in the past, not only in connection with

this case but other litigation, including compensation from other tobacco companies and so forth and so on.

THE COURT: I don't think I required you in regard to other tobacco companies. I think just in regard to -- I can't imagine I would have required you to do it in regard to other tobacco companies. How would you know that.

MR. FINNEGAN: I think the Court said we had to go out and ask these people. That was the Saturday hearing, there was not a transcript of that, but we understood the Court to --

THE COURT: My memory, intent would have been any remuneration from you or from what's the tobacco council?

MR. BRALY: Smokeless Tobacco Company.

MR. FINNEGAN: Smokeless tobacco council.

THE COURT: Counsel, which you are a member.

MR. FINNEGAN: We are a member.

MR. BRALY: They are also a member of the Tobacco Institute, Your Honor, and the council for Tobacco Research.

THE COURT: Go ahead. I think that will be irrelevant. Go ahead with what you were going say.

MR. JENNINGS: We have the information and

we have everything that we can get it for, any other tobacco case or any other tobacco company, because we understood that's what the Court was requiring. Our problem is that we don't feel in fairness to those people that we should disclose information concerning their finances in that they don't, in fact, testify in this lawsuit, and until such --

THE COURT: I'll tell you what. When you decide who is going to testify, you can turn that over, all right?

MR. JENNINGS: All right.

MR. FINNEGAN: Thank you, Your Honor, will that will take care of it.

MR. JENNINGS: That will take care of it. If the Court please, what I would like to do is turn over to them, those that we know now are going to testify.

THE COURT: That's fine, that's fine.

MR. JENNINGS: And the ones that we have not yet, we don't know whether they are or not, there are type problems, we don't know who's going to be available, the ones we don't know about we would rather not turn it over until we know whether they are going to testify.

MR. FINNEGAN: And if the Court please, as

the ruling with the United States Tobacco Company and the Smokeless Tobacco Council --

THE COURT: What is this other officer.

MR. BRALY: Your Honor, they are a member of every one of the industry trade groups and if they have got that information, many of their people who work for the tobacco institute or the council for tobacco research of this company has been a member of all of them.

THE COURT: What I have to say is you don't have to turn it over in regard to other tobacco companies.

MR. FINNEGAN: Thank, Your Honor.

MR. JENNINGS: That will take care of it.

MR. BRALY: But they do as to the trade associations or --

THE COURT: Yes.

MR. BRALY: Okay.

THE COURT: Mr. Braly you had a question about -- let me finish.

MR. BRALY: Sorry.

THE COURT: -- about a deposition that you wanted to use someone to read?

MR. BRALY: It is a minor issue, we have just got somebody over there that's sitting around

waiting to testify, and at some appropriate time, we just want to use him as a reader, that's all.

THE COURT: That's fine.

MR. BRALY: Your Honor, with respect to these payments situations, we have seen some etched that these payments have been coming from law firms representing the council, the tobacco industry agencies, or industry trade groups or from the attorneys representing U.S. Tobacco Company, and we would like to make sure the Court's order is clear that if they have funded these people indirectly through the law firms that that should also be included.

MR. FINNEGAN: If they testified on behalf of the Smokeless Tobacco Council and a payment came from a law firm, that will be included, because, as I understand the Court's ruling, it is if they testified on behalf of the United States Tobacco Company; if they have testified on behalf of the Smokeless Tobacco Council.

MR. BRALY: It is not a question whether they have testified, I am asking for remuneration that they have received from these organizations.

THE COURT: That would be what would be contemplated, any kind of remuneration.

MR. FINNEGAN: Any kind of remuneration that is connected with testimony here requested by tobacco company, U. S. Tobacco Company.

THE COURT: It is clear what you mean, I want remuneration that comes directly or indirectly from United States Tobacco to these witnesses.

MR. BRALY: Does that include the trade organizations?

THE COURT: Yes.

THE CLERK: Bring in the jury?

THE COURT: Yes, bring in the jury.

(The following proceedings were had IN THE PRESENCE AND HEARING OF THE JURY.)

THE COURT: Go ahead, Mr. Braly.

MR. BRALY: Thank you, Your Honor.

Q. (BY MR. BRALY) Doctor Lijinsky, I would like to show an exhibit that has been marked as Plaintiff's Trial Exhibit 97 and the blowup mark as Trial Exhibit 97-A.

A. Thank you.

THE COURT: The blowup is 97-A?

MR. BRALY: Yes, Your Honor.

THE COURT: Plaintiff's 97-A will be admitted. Go ahead.

MR. BRALY: Or 97.

THE COURT: Excuse me.

MR. BRALY: 97 and 97-A.

THE COURT: I am just going to admit one, which one do you want admitted?

MR. BRALY: Well, for the purpose of the record, let's admit the small one.

Q. (BY MR. BRALY) Doctor Lijinsky, have you had a chance to read this document earlier today?

A. Yes.

Q. Why don't I just ask you to go ahead and start in and read the document from the top.

A. From Thomas Ito, director of R & D Services - Greenwich to Tim Cornell, Senior Vice President Manufacturing. And it is headed U.S. Tobacco intra-company correspondence. July the 18th, 1984. N-Nitrosamines are formed by the nitrosation of amines. Tobacco and tobacco smoke contains three types of N-Nitrosamines; volatile nitrosamines, (VNA).

Q. Is that a common abbreviation volatile nitrosamine?

A. Yes, it is commonly used. I don't like that kind of an abbreviation, frankly, but it is often used. "... nitrosamines derived from residues of agricultural chemicals on tobacco, and the tobacco

specific nitrosamines (TSNA). These compounds are formed during tobacco processing and during smoking from precursors such as primary, secondary, and tertiary amines and quaternary ammonium salts, reacting with N-nitrosating agents such as nitrogen oxides, nitrite, and some C-nitro compounds.

"Volatile N-Nitrosamines. A number of volatile N-Nitrosamines" again the abbreviation "VNA, are present in tobacco products and tobacco smoke. The following VNA's have been found in chewing tobacco or snuff:

Nitrosodimethylamine, (NDMA) to 2-56 parts per billion; Nitrosodiethylamine, (NDEA) to 8.6, parts per billion; Nitrosopyrrolidine (NPYR) to 0.5 to 2.0 parts per billion; and Nitrosomorpholine (NMOR), 20 to 700 parts per billion. This high concentration of VNA in snuff is a consequence of the high nitrate levels in the tobacco types used, which ranged from 2 to 5 percent, and the long fermentation times under the anaerobic conditions."

Q. Excuse me, stop there. Referring to the high concentration of VNA that was used by the tobacco company to describe these four nitrosamines, do you agree that those are high concentrations of those nitrosamines?

A. I do.

Q. Okay.

A. "N-Nitrosomorpholine (NMOR) was recently detected" -- I assume "at" there is omitted -- "high levels in snuff. Protein and amino acids serve as the major precursors for most VNA in processed tobacco, but the origin of the precursor for NMOR remains unknown. NMOR is a relatively potent animal carcinogen, including" -- I assume it means inducing -- "primary liver tumors in mice and rats and tumors of the larynx, trachea and lung in Syrian golden hamsters."

Q. Did you agree in NMOR is a relatively potent animal carcinogen?

A. Indeed I do.

Q. Do you know of many more that are more potent?

A. Based on my own study, I don't think there is any that is more potent. (CHECK FOLD 135).

Q. Go ahead.

A. "N-Nitrosodiethanolamine. Among the agricultural chemicals used for the cultivation of tobacco crops are found several amines, amides and carbamates. These include dimethyldodecylamine (PENAR), maleichydrazide diethanolamine, and

carbaryl (SEVIN). Small residual amounts of these agents were found on harvested tobacco. Diethanolamine has been studied as a possible precursor for nitrosodiethanalamine (NDELA), a carcinogen found in tobaccos that were treated with the sucker growth inhibitor maleichydrazide diethanolamine. Snuff has been found to contain 3.2 to 6.8 parts per million NEDLA," I assume that would.

Q. Now, if we translated those into parts per billion, how would you do that?

A. That would be 32 -- 3,200 to 6,800 parts per billion.

Q. Parts per billion. All right.

A. "Tobacco Specific N-Nitrosamines, (TSNA). Commercial tobaccos in the United States contains 0.5 to 2.7 percent alkaloids, 85 to 95 percent of which is nicotine. Important minor alkaloids are nornicotine, anatabine, anabasine, cotinine and then N'- formylnornicotine. Several of these alkaloids are secondary and tertiary amines and, as such, are amenable to N-nitrosation. Chewing tobacco and snuff contain the following:

N-Nitrosonornicotine NNN, 3.5 to 77 parts per million;

4-(methylnitrosamino)-1-(3 pyridyl)-1-tanone

an NNK, 0.8 to 4.7, parts per million;

N'-Nitrosoanatabine NAT, 0.8 to 44 parts per million; and

N'-Nitrosoanabasine NAB, 0.04 to 1.9 parts per million.

Recent studies reported snuff in the United States, Denmark, Germany and Sweden contained 5.5 to 106 parts per million of TSNA. These are the highest levels of carcinogenic nitrosamines reported in the consumer product that is taken into the body. The saliva of Snuff dippers yielded TSNA levels of concentrations of 0.02 to 0.9 parts per million. Researchers feel that TSNA can be formed in the oral cavity during snuff dipping.

Q. Doctor, let's keep these units consistent. If we bring these down and translate into parts per billion, what would they run for NNN and NNK?

A. The 3500 to 77,000 for NNN, NNK 0.8 to 4.7, 800 to 4,700.

Q. NN would be what?

A. That's NNN.

Q. Okay.

A. NNK it would be 800 to 4,700 parts per billion.

Q. Could you make a similar notation on your

original document since that is going to be one that is going to go into the record?

A. All right.

Q. While he is doing that, I will let the jurors at the other end of the room see the document.

Now, Doctor Lijinsky, with respect to this statement in the last paragraph "these are the highest levels of carcinogenic nitrosamines reported in a consumer product that is taken into the body." Based on your knowledge, is that correct, sir?

A. Yes, it is.

Q. Are there any other consumer products that you know of that come anywhere close?

A. Tobacco smoke, if you like to consider that something that is taken into the body.

Q. Anything besides tobacco products that come anywhere close?

A. No.

Q. Doctor, in connection with the experiment you did on Nitrosomorpholine, you testified that some of your laboratory animals at the lower doses had tumors in the oral cavity; is that correct?

A. Yes.

Q. What kind of tumors were they and where were they located?

A. They were squamous cell papillomas and squamous cell carcinomas of the tongue, except in one case, where it was of buccal character.

Q. Like cheek and gum?

A. Yes.

Q. You have got them in both places?

A. Yes, sir.

Q. Have you caused to be prepared some 35 millimeter slides that were taken from those pathology slides in the tongue tissue of those laboratory animals?

A. Yes.

Q. Let me show you what has been marked as Plaintiff's Exhibit 2, it has been already been loaded into this tray, let me ask you if you can identify these three slides as being copies of the originals.

A. Yes, those are copies of the slides.

THE COURT: What is the exhibit number?

MR. BRALY: Trial exhibit 2, A, B and C.

MR. BRALY: Your Honor, we will move the admission of those exhibits 2, A, B and C.

MR. JENNINGS: May we approach the bench, Your Honor

(The following proceedings were had AT THE SIDE

BAR.)

MR. JENNINGS: We object to the introduction of these exhibits, first, as not being a sufficient foundation or identification made of them. Second, they are irrelevant and prejudicial and their prejudicial effect outweighs any relevance or probative value that they might.

THE COURT: What are they?

MR. BRALY: They are slides taken through a microscope, showing the tissue specimens from the squamous cell carcinoma of the tongue in laboratory animals that were introduced by the same carcinogen that is found in snuff. As a matter of fact, they are on the lateral border of the tongue, which is where Sean had his squamous cell carcinoma of the tongue from dipping snuff, this carcinogen in snuff that causes this particular squamous cell carcinoma of the tongue in these laboratory animals.

THE COURT: Well, there has been some question all along as to whether or not these nitrosamines cause cancer to the tongue or tumors in the tongue.

Why wouldn't this be relevant to show that in fact they have on experimental animals?

MR. JENNINGS: He's testified to that, but I

don't think that the photographs are admissible.

THE COURT: Overruled.

(The following proceedings were had IN OPEN COURT.)

Q. (BY MR. BRALY) Doctor Lijinsky, do you know of any product that is designed to be taken into the mouth of human beings that on a routine basis has cancer-causing chemicals as potent as the nitrosamines that are found in Copenhagen Snuff?

A. No.

Q. Do you know of any industry, other than the smokeless tobacco industry, that routinely on a daily basis exposes consumers, people, human beings, to similar quantities of such potent cancer-causing chemicals?

MR. JENNINGS: If the Court please, we object to the form of the question.

THE COURT: Overruled.

A. No, I don't.

Q. (BY MR. BRALY) Do you know of any industry, other than the smokeless tobacco industry, that routinely and on a daily basis invites people through advertising to use products containing similar quantities of such potent causing chemicals as are found in Copenhagen Snuff.

MR. JENNINGS: If the Court please, object to the argumentative nature of the question.

THE COURT: Overruled.

A. No, I don't.

Q. (BY MR. BRALY) Do you know of any industry other than this smokeless tobacco industry that routinely on a daily basis invites people through their advertising to use such products containing such potent cancer-causing chemicals, such as those that are found in Copenhagen snuff?

MR. JENNINGS: The same objection.

THE COURT: I haven't heard the question. Start the question over again.

Q. (BY MR. BRALY) Do you know of any industry, other than the smokeless tobacco industry, that routinely and on a daily basis invites people through advertising to use products containing such potent cancer-causing chemicals such as those found in Copenhagen Snuff without at least placing a simple warning label on the product to warn consumers?

THE COURT: Go ahead.

MR. JENNINGS: We have an objection.

THE COURT: Overruled, overruled.

A. No, I don't.

Q. (BY MR. BRALY) Doctor, would it be

ethically possible, feasible, for any scientist to start an experiment and deliberately give nitrosamines in these levels to human beings for the purpose of conducting scientific research?

A. Not outside a Nazi concentration camp.

Q. In your view, Doctor, is it safe for a corporation to sell the same nitrosamines to human beings in a can of snuff for the purpose of earning a profit?

MR. JENNINGS: The same objection.

THE COURT: Overruled.

A. No, not --

Q. (BY MR. BRALY) Doctor, what if a scientist like yourself gave these cancer-causing chemicals in the laboratory. What is the purpose of all that?

A. To further understand the causes of cancer in humans and to do something about it.

Q. And, Doctor, do you think the nitrosamines in Copenhagen Snuff caused Sean Marsee's cancer?

A. I do. In fact, I think it is the best example of the induction of cancer in a human by nitrosamines.

MR. BRALY: Your Honor, if there is any exhibit that we have failed to offer that has been identified, we would now reurge the admission of that

exhibit, and I have no further questions of this witness this morning.

THE COURT: Cross-examine.

CROSS EXAMINATION

BY MR. JENNINGS:

Q. Doctor Lijinsky, have the animal experiments that have been performed established that nitrosamines is found in tobacco cause oral cancer in human beings?

A. In my opinion, yes.

Q. Do you remember when your deposition was taken?

A. Yes, April this year.

Q. Did you testify at the time of that deposition that it was the epidemiological studies that established that snuff caused oral cancer in human beings and not in laboratory experiments?

A. I said that was one of the indications.

Q. Doctor, do nitrosamines cause cancer in laboratory animals?

A. Yes.

Q. The nitrosamines, themselves, cause cancer?

A. Yes.

Q. Not a metabolite of the nitrosamine?

A. The metabolites of nitrosamines are

themselves nitrosomines.

Q. But the nitrosomines that you are talking about have to be metabolized by the tissue of the animal before they become the metabolite that you feel causes cancer in animals; is that correct?

A. Yes, but the metabolites then are nitrosamines.

Q. But they are not the same nitrosamines?

A. A substance that -- a carcinogen is defined as a substance or an agent that causes cancer in animals or humans. It is a functional definition, a carcinogen. The word "carcinogen" describes not what something is, but what something does.

Q. I understand that, but a carcinogen is not the nitrosamine that you were studying, is it? It is a metabolite of the nitrosamine.

A. I'm afraid I don't understand that question very well, because the metabolite is itself a nitrosamine. It belongs to the same class of substances.

Q. You understand that the nitrosomine has to be metabolized before it becomes carcinogenic in animals; is that not right, Doctor?

A. Oh, yes, I would agree with that.

Q. Isn't that the first question that I asked?

A. I beg you pardon.

Q. Didn't I ask you that several questions ago?

A. Well, I think that the confusion is that amongst the class of nitrosamines, the metabolites do themselves belong to that class, so when you talk about the carcinogen having to be metabolized, the nitrosocompound having to be metabolized to cause cancer, it is metabolilzed to another nitrosomine.

Q. Yes.

A. I don't see -- I don't understand the question very well.

Q. Is it metabolized differently in different species?

A. Sometimes.

Q. Are you aware of metabolization or if that is the correct word and --

A. Metabolism.

Q. Metabolism. And how it works?

A. I know something about metabolism of nitrosomines, yes.

Q. You are familiar with the works of Doctor Hecht?

A. Yes.

Q. Are you familiar with the fact that he has studied metabolism of nitrosamines in animals and in

human tissue?

A. Yes.

Q. And are you familiar with the fact that he has concluded that the metabolism is markedly different in humans than it is in animals?

A. In some respects.

Q. And what is different?

A. Portions of products are formed, sometimes different products are formed when we talk about metabolism of compound, we look for the -- we are able to examine the major metabolites. There are pathways of metabolism that occur that we are unable to study because they occur at such a low level. We don't know very much about the mechanism by which carcinogens induce cancer.

Q. You have told me I believe in your deposition that you had read the Hecht deposition.

A. Yes.

Q. And then did you read the part in his deposition when he said "in comparing the results from human and experimental animal tissues, we observed both quantitative and qualitative differences in metabolism"?

A. May I see that.

Q. Sure.

(Handed to the witness)

A. Thank you. Yes.

Q. Do you recall reading that?

A. Yes.

Q. Do you recall that he also said "the conversion of NNN to metabolites up to .8 percent was considerably lower in human tissues compared to those from experimental animals (30 to 60 percent)"?

A. I don't recall -- I don't recall reading that, but if you show me, I will --

MR. JENNINGS: Do we have another copy?

A. Sorry. You will get good exercise.

Q. I need it.

A. Yes.

THE COURT: Here's an extra copy. Are you talking about Hecht?

MR. JENNINGS: Hecht.

A. Okay. Thank you.

MR. JENNINGS: If the Court please there are only a few more questions from this deposition. We can go ahead.

MR. JENNINGS: Maybe if I can approach the witness, Your Honor.

THE COURT: That's fine.

MR. JENNINGS: I'm sorry.

Q. (BY MR. JENNINGS) Did Doctor Hecht testify further "The distribution of metabolites was also quite different"?

A. Yes.

Q. "For example, in the human esophagus N-oxidation was observed to a greater an extent than was five --"

A. Hydroxylation.

Q. " -- hydroxylation. And two-hydroxylation was not detected"?

A. Yes, yes.

Q. "In contrast to hydroxylation was the major metabolic pathway in rat esophagus and five-hydroxylation was the predominant mode of metabolism in hamster esophagus."

A. Yes.

Q. "Since human tissues can metabolically carry out the A-hydroxylation of NNN, they can be considered as potential target tissues. However, the observed differences in regiospecificity specificity between the human and animal tissue in NNN metabolism suggests that NNN may have different target organs in man and experimental animals"; is that right?

A. That's what he says.

Q. And do you disagree with him?

A. I don't agree with what he says is fact. I disagree with his interpretation -- or I don't entirely agree with his interpretation, because we don't know the mechanism by which nitrosonornicotine or any other carcinogen causes cancer.

Q. You say you don't know how any of them cause cancer?

A. No, we don't know the mechanism by which any carcinogen causes cancer.

Q. And as far as human beings are concerned, you don't know whether they cause cancer, do you?

A. Yes, we do.

Q. From what source?

A. From analgies to humans -- analgies to experimental animal studies from epidemiological studies.

Q. Epidemiological studies --

A. Yes, sir.

Q. -- are a necessary element, are they not?

A. Not absolutely necessary, no.

Q. Suppose all the epidemiological studies failed to show any connection, then what?

A. I'd have to have -- I'd have to read the studies, I'd have to consult with an epidemiologist I trust to find out whether or not these studies were

valid in that conclusion.

Q. I understand that, Doctor. The validity of studies would be the a question, of course.

A. Yes.

Q. But the epidemiological studies did not show the association between the product and cancer, then you could not say that it had been established that the product caused the cancer, could you?

A. By epidemiological studies, no.

Q. Epidemiological studies are an important part of it, aren't they?

A. They are important, but not essential.

Q. Not essential?

A. No.

Q. You can establish it without the epidemiological studies.

A. Based on -- that's the reason I do my animal experiments.

Q. Then if the epidemiological studies showed to the contrary but didn't agree with the conclusion that you reached from the animal studies, what would you do?

A. I would have to make sure that the epidemiological studies were trustworthy first.

Q. But if they don't support you, then you

ignore them?

A. I'm sure epidemiological studies have been done --

Q. Yes?

A. -- which have failed to show a relationship between exposure to a carcinogen and a particular human cancer, but that isn't a valid way, knowing how -- knowing all the differences in all of the organ specificities to do such epidemiological studies and reach that conclusion.

Q. Doctor, my question is if the epidemiological studies don't bear out the conclusion you reached from your experimental studies, then what do you do?

A. I'd have to examine the study before I could reach that conclusion. You are making an hypothesis --

Q. Yes.

A. -- that I don't accept. I want to see the studies before I make the judgment.

Q. I understand you quarrel with the hypothesis, but if the hypothesis is correct, is the conclusion correct?

A. I'm sorry. Would you repeat that?

Q. I know you won't accept my hypothesis, but

if my hypothesis is correct, then is the conclusion correct that your opinion based solely on experimental animals needs to be re-examined?

A. It might have to be re-examined.

Q. Thank you, sir. Now, tell me this. How much experimentation have you done with snuff?

A. None.

Q. Absolutely none, have you?

A. Absolutely none.

Q. Do you know of experimentation with animals with snuff?

A. I have not done any experimentation with animals with snuff.

Q. Are you aware of experimentation that has been done with animals with snuff?

A. Yes.

Q. What has been the result of that experimentation?

A. Some of the results show the induction of tumors in animals exposed to snuff.

Q. What experiments show that?

A. I think the experiments of Hoffmann, Park, Hirsch. I'm not -- this is not my particular area. I have read some of these papers, but I don't know them in detail.

Q. You are aware, of course, that Park and Hirsch did experiments using herpes simplex virus and snuff?

A. Yes.

Q. And you are aware, I am sure, that Park did experiments with snuff alone and Hirsch has done experiments with snuff alone and have not produced any cancer in the experimental animals; is that correct? Are you aware of that?

A. They produce tumors.

Q. They produced tumors?

A. Yes.

Q. The snuff alone?

A. Tumors.

Q. Are you aware of that?

A. I seem to recall -- I could -- I could be wrong, but I think I recall that they produced tumors.

Q. You think you recall that, but you are not sure; is that right?

A. Not absolutely certain.

Q. You say Hoffmann produced tumors with snuff, alone?

A. No, snuff extract.

Q. Snuff extract?

A. Yes.

Q. Tell me about that experiment.

A. I think the experiment he -- in which he swabbed out the mouth of hamsters with an extract of snuff produced some tumors.

Q. How many?

A. How many?

Q. Yes, sir.

A. I don't remember. A few, two, I think, two or three.

Q. A significant number of tumors?

A. Strictly speaking, no, but considering that we rarely, very, very rarely see a tumor of the oral cavity that is not induced by exposure to carcinogenic nitrosamine, I would -- I would consider even two an indication of carcinogenicity.

Q. What you are telling me is that these animals do not have spontaneous tumors?

A. Very rarely have tumors of the oral cavity.

Q. What you are telling me is that if you have an experiment and you have control animals --

A. Yes.

Q. -- who are not getting whatever the substance is that you are testing that you don't get tumors in the control animals; is that right?

A. You might get -- you might occasionally get one, very, very rarely. You might occasionally get one.

Q. So that is the reason that you say if you get one tumor in the animal that is getting the substance, that is not statistically significant because you might get one in the animal that is not getting the substance; is that correct?

A. Yes, yes.

Q. Now, would you consider that the human population that doesn't use tobacco would constitute a sort of control group like your rats that are not getting the product?

A. I don't understand --

Q. In your experimental studies you have the users and the nonusers --

A. Yes.

Q. -- and you call the nonusers the control?

A. Right.

Q. Now, would you say that in the human population that the nonusers of tobacco would constitute the control group for comparison purposes?

A. It's not a strict control group, because it is not genetically homogeneous, not genetically

comparable.

Q. Let me ask you this. If you had 20 rats --

A. Yes.

Q. -- and you had 20 control rats and you gave the 20 rats whatever you want to test, nitrosamines or whatever, and you gave the 20 control rats nothing, gave them none of that, they would be nonusers of that particular substance, and you got five cancers in your test animals and you got all 20 cancers, got 20 cancers in your nontest, in your control group, what would you think of that?

A. You got five cancers in the nontest animals?

Q. Yes.

A. Five in the test group?

Q. Yes, yes.

A. And 20 in the nontest group?

Q. Yes.

A. I would think that would be a highly unlikely outcome.

Q. Oh, I know it is highly unlikely. Suppose it happens.

A. I have never seen in my entire experience such a thing happen.

Q. Well, suppose you had five tongue cancers in people in age ranging from 11 to 17 and four of them

had never used tobacco in any form and one had used chewing tobacco for one year. What would that prove?

A. In itself it wouldn't prove anything one way or the other.

Q. Would it prove that the one who had been using tobacco had his cancer caused by tobacco?

A. It certainly is a possibility.

Q. Would it prove that?

A. No, it won't prove it, but it certainly would still be a possibility.

Q. Would it suggest to you, that particular fact situation, suggest to you that the one who used tobacco had his cancer caused by tobacco?

A. Of course.

Q. What about the other four?

A. I beg your pardon?

Q. What about the other four?

A. Their cancer was caused by -- was caused by something else.

Q. Wouldn't you consider it significant that there were four people who had their cancer caused by something else?

A. No.

Q. It wouldn't mean a thing to you?

A. No.

Q. You still say that the one who chewed tobacco had his cancer caused by chewing tobacco?

A. That's right, because tobacco, chewing tobacco contains carcinogenic nitrosamines that cause cancer.

Q. Well, evidently there is something else out there that is causing cancer, isn't there?

A. Possibly, yes.

Q. Not possibly. You got four cases of people who don't use tobacco out of these five that I am talking about. You know tobacco didn't cause those four, don't you?

A. If you tell me so.

Q. Well, I am asking you to -- incidentally, do you ever read any of the literature?

A. I have read some of it, but not very -- since it is not my area of research, I have not read it very inclusively.

Q. And you read Doctor Patel's article in which he described the five youngsters in India over a period of five years they found in their institution?

A. Looks like eight, but I don't remember any details of that paper.

Q. Well, assuming that Doctor Patel so reported and assuming that he had five cases, four of them had

never used tobacco in any form and one had used tobacco for one year, you would come into this court and testify that that one cancer was caused by tobacco?

A. It may -- I believe that the use of tobacco by that person contributed to his cancer.

Q. And then again I ask you how did the other four get cancer?

A. I don't know.

Q. Right. And if you don't know what caused their cancer, you don't know what caused the fifth one's cancer, do you?

A. I know that the carcinogenic nitrosamines in tobacco produce cancer.

Q. You know that?

A. Yes.

Q. Does snuff produce cancer?

A. Yes.

Q. Are you familiar with the unpublished article by Doctor Hecht, the one that he submitted for publication in, I believe, January of this year? You are familiar with that, aren't you?

A. I can't recall it.

Q. You testified about it in your deposition, didn't you?

A. Which particular article? Can I see the article?

Q. You certainly may.

(Handed to the witness).

A. Yes.

Q. Are you thoroughly familiar with that article?

A. I'd have to reread it. Yes, now I recall it.

Q. Why don't you use that copy, Doctor Lijinsky?

A. Fine.

Q. Turn to page 11.

A. Yes.

Q. And at the bottom of the page the paragraph that begins about seven lines from the bottom of the page on Page 11?

A. Yes.

Q. I will read that to you.

A. Okay.

Q. "Whereas the incidence of oral cavity tumors was out of 30 and in the rats treated with NNN and NNK, it was only three out of 30 in the rats treated with snuff extract enriched with NNN and NNK. This difference was not statistically significant, but

taken together with the negative results obtained in the animal swabbed with snuff extract only, it suggests that NNN and NNK were less tumorigenic when administered together with snuff extract than when administered alone. This might in part be associated with a significantly lower weight of the animals in Group Two and Three compared to those in Group 4, suggesting a general toxic effect of snuff extract perhaps due to nicotine. It is also possible that nicotine, which is present in great excess over NNN and NNK even in the enriched extract might act as a competitive inhibitor of their metabolic activation in the oral mucosa. Furthermore, snuff extract may contain other inhibitors of NNN and NNK activation as shown for a number of other plant-derived compounds. Studies are required to elucidate the mechanism of the apparent inhibitory effect of snuff extract on NNN and NNK tumorigeneses in the rat oral cavity."

Did you read that?

A. Yes.

Q. Do you agree with that?

A. I agree that that's one possibility.

Q. You think it is a possibility that snuff inhibits the carcinogenicity of the nitrosamines; is that right?

A. Nicotine in snuff.

Q. Nicotine?

A. The nicotine in snuff.

Q. Nicotine in stuff inhibits the carcinogenicity of the nitrosamines?

A. In that particular circumstance of their experiment, this is one interpretation or of that result.

Q. All right, sir. Which means that testing the product snuff is something totally different from just testing nitrosamines which incidentally you didn't get out of snuff but which you synthesized in the laboratory; is that right?

A. Is what right?

Q. That you may get an entirely different result when you use the snuff itself than you get when you just use nitrosamines?

A. They are not entirely different; they are marginally different.

Q. You might get a different result --

A. Yes.

Q. -- with the product than you would get with the nitrosamines?

A. Slightly different.

Q. Sir?

A. Slightly different.

Q. Slightly different?

A. Yes.

Q. Well, in this instance you get no tumors, you know they got no tumors with the snuff, don't you?

A. Yes.

Q. And you get tumors with the nitrosamines by themselves?

A. Yes. Quite a different -- quite a different experimental arrangement when you insert a solid like snuff into an animal -- into a -- I think it is a surgically-made pouch and you leave it there, and giving the -- giving the animals a solution of a nitrosamine, the dynamics of the carcinogenic action are different. This is an experimental animal model which might not at all resemble or mimic human experience.

Q. I understand that. All of them are experimental models that might have no relevance whatsoever to human experience?

A. I didn't say they might not have no relevance. I said they might not mimic exactly.

Q. The fact of the matter is that when they gave the animals snuff, they didn't get tumors, and

when they gave them NNN and NNK without snuff, they did get tumors, and when they gave them snuff and NNN and NNK, they got fewer tumors than if they gave them NNK and NNN alone; is that right?

A. Yes.

Q. So that would indicate that the product itself doesn't have the same causal effect as maybe the NNN and NNK has on these animals; is that right?

A. Not exactly the same.

Q. Well, not anything close to the same, none as opposed to some. There were no tumors with the snuff alone?

A. Right.

Q. And there were tumors with NNN and NNK alone. That's quite different, isn't it?

A. Yes.

Q. So it is not just a little different? It is a marked difference, isn't it?

A. The amounts are different. The dose is different. The dose is quite different.

Q. I understand that, but I am asking you if experimentation seems to establish that the result you get from the product is different from the result you get from synthesized NNN or NNK that you used alone?

A. But the doses are different. That's the reason the results --

Q. Is that the explanation of why they are different?

A. I think so.

Q. Then the dose in the snuff is not sufficiently large to cause cancer in the animal; is that right?

A. In this particular animal protocol, in this particular experimental protocol it was not enough.

Q. It had to be enriched ten times in order to cause tumors in the ones that used snuff and the nitrosamines; is that right?

A. Within that time span of the experiment.

Q. So that is your explanation is that the dosage just wasn't sufficient in the snuff alone?

A. In this particular case, in this particular experimental protocol.

Q. But in some other case the amount of the snuff alone would be sufficient?

A. If you could design an experiment to properly mimic the use of snuff by humans, if you could design in rats such an experiment, I think you would produce tumors.

Q. Doctor Lijinsky, when did you first meet Mr.

Braly?

A. I think it was February, 1984, if I am not mistaken.

Q. That would be two-and-a-half --

A. Yes.

Q. Not two-and-a-half, a little over two-and-a-third years ago.

A. Yes.

Q. And I believe that before your deposition was taken that you and Mr. Braly, according to what you told me, spent about seven hours together; is that right?

A. Yes, sir.

Q. And how much time have you and Mr. Braly spent together preparing for your testimony here?

A. We spent about, I would say, four hours yesterday, yesterday evening. I don't remember exactly, because other -- we talked about other things. We had a social meeting as well with dinner and, we talked about other things apart from this case and nitrosamines. I think it was about four hours.

THE COURT: Mr. Jennings, I assume you will be with this witness for a while?

MR. JENNINGS: Yes, sir.

THE COURT: Any problem breaking now?

MR. JENNINGS: Fine.

THE COURT: All right.

Let's take a recess now, ladies and gentlemen, until 1:30. Remember, don't make up your mind in the case until you have heard all of the evidence and don't read or listen or discuss the case outside the courtroom, and we will see you back at 1:30.

Everyone remain seated while the jury exits to 1:30.

Court will be in recess.

(The noon recess was here had.)